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The importance of extra care for parathyroid gland secure during total thyroidectomy

Parathyroid glands secure during total thyroidectomy

Ayetullah Temiz
Department of General Surgery, Erzurum Regional Training and Research Hospital, Erzurum, Turkey

Abstract

Aim: One of the most common complications after thyroid surgery is hypocalcemia. Hypocalcemia can be seen transiently or permanently. In this study, we aimed to reveal the factors affecting the development of hypocalcemia in patients who underwent total thyroidectomy. Material and Method: The files of the patients who underwent thyroidectomy between September 2009 and December 2014 were reviewed retrospectively. Patient files were reviewed for age, gender, thyroid function tests, postoperative calcium values, pathology reports and peroperative parathyroid auto-implantation. Patients were grouped according to the presence of transient and permanent hypocalcemia. The effects of the obtained data on the effects of transient and permanent hypocalcemia were investigated. Results: Eight hundred and twenty-four patients were included in our study. The mean age of the patients was 46.56 ± 12.52. Of the patients, 115 (14%) were male and 709 (86%) were female. While the incidence of permanent hypocalcemia was 1.3%, the incidence of transient hypocalcemia was 27.3%. Factors affecting the development of transient hypocalcemia were female gender ($p < 0.001$), hyperthyroidism ($p < 0.001$), parathyroid auto-implantation ($p = 0.001$), and incidental parathyroid excision ($p < 0.001$). The only factor affecting the development of permanent hypocalcemia was incidental parathyroid excision ($p < 0.001$). Discussion: Incidental parathyroid excision has an effect on the development of both transient and permanent hypocalcemia, whereas sex, hyperthyroidism, and parathyroid auto- implantation have an effect on transient hypocalcemia.

Keywords

Total Thyroidectomy; Transient Hypocalcemia; Permanent Hypocalcemia; Parathyroid Excision; Parathyroid Auto-Implantation

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Corresponding Author: Ayetullah Temiz, Department of General Surgery, Erzurum Area Training and Research Hospital 25100 Erzurum, Turkey.
T.: +90 4422325248 E-Mail: temiz-49@hotmail.com
ORCID ID: https://orcid.org/0000-0003-2178-3369

Introduction

Total thyroidectomy is the standard surgical procedure for benign multi-nodular goiters and malign diseases of the thyroid gland [1]. Surgical treatment should allow both the treatment of the disease and the minimization of postoperative complications [2]. The most common postoperative complications are hemorrhage, hypoparathyroidism, and related hypocalcemia and recurrent laryngeal nerve injury. Hypocalcemia is one of the common complications in postoperative period and develops postoperatively 24-48 hours [3]. The causes of the postoperative hypocalcemia are not fully known but are considered to be multifactorial. In this study, we aimed to investigate the rates of postoperative temporary or permanent hypocalcemia and factors affecting hypocalcemia in 824 patients who underwent thyroidectomy due to thyroid disease in the general surgery clinic of a regional hospital with a high number of patients

Material and Method

The files of the patients who underwent thyroidectomy in our General Surgery Clinic between September 2009 and December 2014 were reviewed retrospectively. Age, gender, routine laboratory examinations, preoperative ultrasonography findings, thyroid function tests, thyroid scintigraphy, performed operation, whether parathyroid damage occurred during the surgery or not, whether parathyroid auto-implantation was performed (implantation of the incidentally removed parathyroid gland into the sternocleidomastoid (SCM) muscle) or not, postoperative thyroid histopathology results, and whether incidental parathyroidectomy was performed or not were recorded from patient files. Serum total calcium was examined in patients who developed hypocalcemia symptoms (paresthesia in the extremities and around the mouth, Chvostek and Trousseau findings) on postoperative 1st and 2nd day. Patients with a calcium level of less than 8.5 mg/dl were considered as transient hypocalcemia. These patients were followed for 12 months. Improvement in hypocalcemia at the end of six months was considered as transient hypocalcemia and continued hypocalcemia at the end of one year was considered as permanent hypocalcemia. Transient and permanent hypocalcemia rates were statistically compared in terms of age, gender, hormonal status, incidental parathyroidectomy, peroperative parathyroid auto-implantation, and histopathological diagnosis.

According to the clinical data of the patient, oral or intravenous vitamin D + calcium replacement was performed in patients who developed hypocalcemia in the postoperative period. During the operation, parathyroid auto-implantation into the right SCM muscle was performed to 90 patients who were noticed to have been undergone iatrogenic parathyroidectomy. Patients who underwent central or lateral neck dissection due to subtotal thyroidectomy, lobectomy or malignancy were excluded from the study. The study was designed in conformity with the Declaration of Helsinki. There was no need for ethical approval because this is a retrospective study.

Results

Eight hundred and twenty-four patients who underwent thyroidectomy surgery were included in this study. The general demographic characteristics of the patients included in the study are given in Table 1. According to these findings, the mean age of the patients was 46.56 ± 12.52, 115 of them (14%) were male and 709 (86%) were female patients. According to pathology results, 592 patients were benign, 116 patients were malign and 116 patients were thyroiditis. Hyperthyroidism was seen in 5% of the patients. The number of the patients with parathyroid auto-implantation was 90 and the number of the patients with incidental parathyroid excision was 65 (7.9%). The incidence of permanent hypocalcemia was 1.3% and the incidence of transient hypocalcemia was 27.3%. Factors, affecting permanent hypocalcemia are summarized in Table 2. According to the results, there were no statistically significant

Table 1. General demographic characteristics of patients

Variable	n	%
Age	46.56 ± 12.52	
Sex		
Male	115	(%14)
Female	709	(%86)
Histopathology		
Nodular / adenomatous goiter	592	(%71,8)
Malignancy	116	(%14.1)
Thyroiditis	116	(%14.1)
Hyperthyroidism		
Yes	41	(%5)
No	783	(%95)
Hypocalcemia		
No	588	(%71.4)
Transient	225	(%27.3)
Permanent	11	(%1.3)
Incidental parathyroidectomy		
Yes	65	(%7.9)
No	759	(%92.1)
Parathyroid auto-implantation		
Yes	90	(%10.9)
No	734	(%89.1)

Table 2. Analysis of factors affecting permanent hypocalcemia

Permanent Hypocalcemia			
Factors	Yes (n=11)	No (n=813)	p
Age	38.73±10.51	46.79±10.80	0.756
Sex			0.532
Male	1	114	
Female	10	699	
Histopathology			0.847
Nodular / adenomatous goiter	8	584	
Malignancy	4	114	
Thyroiditis	1	115	
Hyperthyroidism			0.100
Yes	2	39	
No	9	774	
Incidental parathyroidectomy			<0.001
Yes	11	54	
No	0	759	
Parathyroid auto-implantation			0.109
Yes	3	87	
No	8	726	

differences between the patients with and without permanent hypocalcemia in terms of gender, operation type, pathology result, the condition of hyperthyroid and parathyroid implantation (p-values are 0.756, 0.532, 0.862, 0.847, 0.100 and 0.109, respectively). Incidental parathyroid excision had a statistically significant effect on the development of permanent hypocalcemia (p <0.001).

The factors affecting transient hypocalcemia are summarized in Table 3. According to the results, there were no statistically significant differences between the patients with and without transient hypocalcemia in terms of age, operation type and pathologic results (p-values are 0.240, 0.193 and 0.095, respectively). The rate of transient hypocalcemia was higher in female gender (p <0.001). Most of the patients with hyperthyroidism had transient hypocalcemia and this was statistically significant (p <0.001). Incidental parathyroid excision had a statistically significant effect on the development of transient hypocalcemia (p <0.001). It was also found that parathyroid auto-implantation did not improve the transient hypocalcemia.

Table 3. Analysis of factors affecting transient hypocalcemia

Transient Hypocalcemia			
Factors	Yes (n=236)	No (n=588)	p
Age	44.67±12.92	46.95±13.01	0.240
Sex			<0.001
Male	16	99	
Female	220	489	
Histopathology			0.095
Nodular / adenomatous goiter	161	431	
Malignancy	43	73	
Thyroiditis	32	84	
Hyperthyroidism			<0.001
Yes	41	0	
No	195	588	
Incidental parathyroidectomy			<0.001
Yes	40	25	
No	196	563	
Parathyroid auto-implantation			0.001
Yes	40	50	
No	196	538	

Statistical Analysis

Data were analyzed using the SPSS (Statistical Package for Social Science) for Windows 19.0 package program. Data normality was tested by a one-sample Kolmogorov- Smirnov test. Continuous variables were reported as the mean ± standard deviations and were compared using Kruskal-Wallis variance analyses. Dunn's test was used for post-hoc tests after the Kruskal-Wallis test. Non-continuous variables were reported as medians (min-max) and were compared using the Chi-Square test. P-values of less than 0.05 were considered significant.

Discussion

Hypocalcemia after thyroid surgery is an important problem and can lead to serious complications. Whereas hypocalcemia is temporary and heals in most patients, hypocalcemia can be permanent if the parathyroid glands are permanently damaged [4,5]. Hypocalcemia can be symptomatic in the early period as well as after discharge. Therefore, both the treatment and hospitalization times of patients can be prolonged [6]. In the literature, postoperative hypocalcemia rates after total thyroidectomy were reported to be between 1.6- 40% [7,8] and permanent hypocalcemia rates between 0.6-4.7% [7,9,10]. Our study was consistent with the literature, as the rate of transient hypocalcemia was 27.3% and the rate of permanent hypocalcemia was 1.3%.

Age and gender are among the most patient-related factors. In the literature, data about the relationship between transient hypocalcemia and age are incompatible. There are some studies reporting that transient hypocalcemia is related to advanced age [11] but also there are some studies reporting that it is associated with young age [12]. Edafe et al.'s [13] meta-analysis showed no significant difference in the mean age between patients with and without transient hypocalcemia. In our study, both permanent and transient hypocalcemia were observed more frequently in younger patients, but there was no significant relationship between gender and hypocalcemia.

In some studies, it is stated that gender is a risk factor for hypocalcemia. Thomusch et al. [14] in their study reported that women have higher rates at both permanent and transient hypoparathyroidism. In a study conducted in our country, the rate of hypocalcemia in males was 11.6% and in females this rate was found to be 27.5% and the ratio was found statistically significant [15]. Unal et al. [16] in their study on 1022 patients found that the rate of transient and permanent hypocalcemia was significantly higher in women. In this study, gender was found to be an important risk factor for hypocalcemia. The estimated relative risk at the logistic regression model was determined as 4.246. In our study, the relationship between persistent hypocalcemia and gender was not statistically significant, the incidence of transient hypocalcemia in males was 14% and the incidence in females was 31%, and this ratio was statistically significant. We think the reason of the higher frequency of hypocalcemia in women can be due to the fact that women are more affected from surgical stress psychologically when compared to men. We think that the effect of this psychological state on the calcium metabolism needs to be investigated.

One of the most important factors affecting preoperative hypocalcemia in the literature is that the patients with hyperthyroidism are being euthyroidized and then be operated [17,18,19,20]. Accumulation of calcium in bones in hyperthyroid patients may cause a decrease in serum calcium. When normal parathyroid function is proved, this "hungry bone syndrome" appears to be the most likely cause of hypocalcemia [4]. In addition, another cause of hypocalcemia in patients with hyperthyroidism is that the parathyroid glands may become ischemic or damaged during dissection because the thyroid gland has a lot of blood flow and adhesions. In our study, 41 (5%) patients were hyperthyroidic and 783 (95%) were euthyroidic in the preoperative period. The rate of hyperthyroidism was significantly higher in patients with postoperative transient hypocalcemia than in those without hypocalcemia.

Hypocalcemia rates in patients who underwent total thyroidectomy due to malignancy were found to be between 0.6-25% [21-23]. In these patients, the parathyroid glands are at a higher

risk of injury, because the posterior capsule of the thyroid is also removed [24, 25]. In our study, malignancy was detected in 14.1% of the patients in histopathological evaluation. Transient hypocalcemia developed in 37% of these patients and this ratio was not statistically significant.

One of the most important causes of hypocalcemia in patients who underwent total thyroidectomy is the peroperative iatrogenic removal of parathyroid glands or damage due to devascularization. If the damaged or excised parathyroid gland is noticed during operation, autotransplantation into the SCM is recommended [25,26]. Sometimes this condition is not noticed but it can be seen incidentally through histopathological evaluation. In recent studies, the frequency of incidental parathyroidectomy rates vary between 5.2% and 26% [27,28]. In the literature, in patients with incidental parathyroidectomy, the rate of transient hypocalcemia is 66.3% and the rate of permanent hypocalcemia is 8.1% [29]. In our study, incidental parathyroidectomy is detected in 7.9 % of the patients. Transient hypocalcemia was detected in 61.5% and permanent hypocalcemia was detected in 16.9% of these patients. The relationship between incidental parathyroidectomy and both transient and permanent hypocalcemia was statistically significant. In addition, in our study, we noticed iatrogenic parathyroidectomy was performed in 90 (10.9%) patients intraoperatively and parathyroid autoimplantation into the right SCM muscle was performed. Transient hypocalcemia was developed in 40 (44%) and permanent hypocalcemia was developed in 3 (3.3%) among the patients with parathyroid auto-implantation. The relationship between parathyroid auto-implant and transient hypocalcemia was statistically significant at a significant level, but the relation between permanent hypocalcemia was not statistically significant. Zedenius et al. [30] in their study showed that auto-implant has removed permanent hypocalcemia in 100 patients with total thyroidectomy. In two studies, the rates of transient hypocalcemia in patients who underwent parathyroid auto-implantation were 16.8-26.5% respectively and studies showed that auto- implantation reduced the rate of permanent hypocalcemia to 0.3-0.9% respectively and removed permanent hypocalcemia as 100% [31,32]. In our study, we observed that parathyroid auto implantation did not remove transient hypocalcemia but permanent hypocalcemia did not develop in these patients. We recommend parathyroid auto-implantation because it prevents permanent hypocalcemia.

In conclusion, according to the results of our study, while gender, hyperthyroidism, and parathyroid auto-implantation have an effect on transient hypocalcemia, incidental parathyroid excision affects both transient and permanent hypocalcemia development. We recommend careful and sensitive dissection in risky patients such as hyperthyroidism and parathyroid auto-implantation when it is noticed. We also recommend examination of the specimen for parathyroid after the specimen is removed and auto-implantation of iatrogenic excised parathyroid glands on the specimen in terms of incidental parathyroidectomy.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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